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(54) Title: MUTATIONS IN NOD2 ARE ASSOCIATED WITH FIBROSTENOSING DISEASE IN PATIENTS WITH CROHN'S DISEASE

(57) Abstract: The present invention provides a method of diagnosing or predicting susceptibility to a clinical subtype of Crohn's disease characterized by fibrostenosing disease by determining the presence or absence in an individual of a fibrostenosis-predisposing allele linked to a NOD2/CARD15 locus, where the presence of the fibrostenosis-predisposing allele is diagnostic of or predictive of susceptibility to the clinical subtype of Crohn's disease characterized by fibrostenosing disease. In a method of the invention, the clinical subtype of Crohn's disease can be, for example, characterized by fibrostenosing disease independent of small bowel involvement. The invention also provides a method of optimizing therapy in an individual by determining the presence or absence in the individual of a fibrostenosis-predisposing allele linked to a NOD2/CARD15 locus, diagnosing individuals in which the fibrostenosis-predisposing allele is present as having a fibrostenosing subtype of Crohn's disease, and treating the individual having a fibrostenosing subtype of Crohn's disease based on the diagnosis.

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# INTERNATIONAL SEARCH REPORT

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| <b>A. CLASSIFICATION OF SUBJECT MATTER</b>  |  |  |  |   |   |  |   |  |  |   |  |  |
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| According to International Patent Classification (IPC) or to both national classification and IPC   |  |  |  |   |   |  |   |  |  |   |  |  |
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| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  |  |  |  |   |   |  |   |  |  |   |  |  |
| <b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>   |  |  |  |   |   |  |   |  |  |   |  |  |
| Category *  | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No.  |  |   |   |  |   |  |  |   |  |  |
| X   | Abreu et al. "Mutations in NOD2 are associated with fibrostenosing disease in patients with Crohn's disease." Gastroenterology. April 2002. Vol. 122, No. 4, Suppl. A29.   | 1-23   |  |   |   |  |   |  |  |   |  |  |
| X,P   | Abreu et al. "Mutations in NOD2 are associated with fibrostenosing disease in patients with Crohn's disease." Gastroenterology. September 2002. Vol. 123, No. 3, pages 679-688.  | 1-23   |  |   |   |  |   |  |  |   |  |  |
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